

wherein

X is HO-NH- or HO-;

R_1 is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, 4-cyanophenyl, benzamido and benzamido substituted on the terminal phenyl ring by C_1 - C_4 alkyl, fluoro, chloro, cyano or C_1 - C_4 alkoxy;

R_2 is selected from:

(a) -S-Ar or -S-CH₂-Ar, wherein Ar is a monocarbocyclic or bicarbocyclic aromatic moiety which is either unsubstituted or substituted with one or two substituents selected from C_1 - C_4 alkyl, phenyl, benzyl, C_1 - C_4 alkoxy, fluoro, chloro, bromo, nitro, cyano, hydroxy, amino, dimethylamino, acetamido, methylthio and acetyl;

(b) -O-Ar, wherein Ar is as defined above;

(c) -S-Het or -S-CH₂-Het, wherein Het is a heterocyclic ring selected from pyridine, pyrimidine, pyridazine, pyrazine, 1,2,5-triazine, imidazole, thiophene, furan, pyrrole, pyrazole, 1,3-thiazole, 1,3-oxazole, 1,2,3-triazole, 1,2,4-triazole, 1,3,4-thiadiazole, 1,3,4-oxadiazole, 1,2,3,4-tetrazole, quinoline, isoquinoline, indole, 1,3-benzoxazole, 1,3-benzothiazole, benzimidazole, [1,3]oxazolo[4,5-b]pyridine, [1,3]thiazolo[4,5-b]pyridine, [1,2,3,4]tetrazolo[1,5-b]pyridazine and purine, and wherein said Het group can be substituted with one to three substituents selected from C_1 - C_4 alkyl, phenyl, pyridyl, benzyl, C_1 - C_4

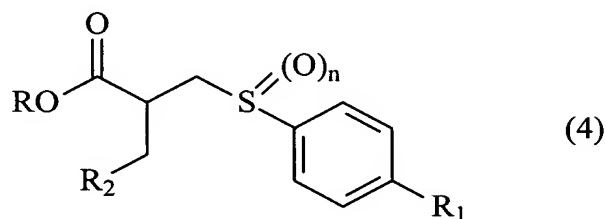
alkoxy, methylthio, fluoro, chloro, nitro, cyano, hydroxy, oxo, amino, methylamino, dimethylamino, 2-dimethylaminoethyl, acetamido and acetyl; and

(d) 2,5-dioxo-1-imidazolidinyl or 2,4-dioxo-1-imidazolidinyl, either of which is

A¹ optionally substituted at the carbon atom by one or two methyl, linear or branched C₂-C₄ alkyl, phenyl, benzyl or hydroxymethyl groups, and at the nitrogen atom with C₁-C₄ linear or branched alkyl;

or a pharmaceutically acceptable salt thereof.

4. (Amended) A process for producing a compound as defined in claim 1, starting from a compound of formula 4:



wherein R is H or the residue of a carboxylic acid ester, R₁ is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, 4-cyanophenyl, benzamido and benzamido substituted on the terminal phenyl ring by C₁-C₄ alkyl, fluoro, chloro, cyano or C₁-C₄ alkoxy;

R₂ is selected from:

(a) -S-Ar or -S-CH₂-Ar, wherein Ar is a monocarbocyclic or bicarbocyclic aromatic moiety which may be either unsubstituted or substituted with one or two substituents selected from the group consisting of C₁-C₄ alkyl, phenyl, benzyl, C₁-C₄ alkoxy, fluoro, chloro, bromo, nitro, cyano, hydroxy, amino, dimethylamino, acetamido, methylthio and acetyl;

(b) -O-Ar, wherein Ar is as defined above;

(c) -S-Het or -S-CH₂-Het, wherein Het is a heterocyclic ring selected from the group consisting of pyridine, pyrimidine, pyridazine, pyrazine, 1,2,5-triazine, imidazole, thiophene, furan, pyrrole, pyrazole, 1,3-thiazole, 1,3-oxazole, 1,2,3-triazole, 1,2,4-triazole, 1,3,4-thiadiazole, 1,3,4-oxadiazole, 1,2,3,4-tetrazole, quinoline, isoquinoline, indole, 1,3-benzoxazole, 1,3-benzothiazole, benzimidazole, [1,3]oxazolo[4,5-b]pyridine, [1,3]thiazolo[4,5-b]pyridine, [1,2,3,4]tetrazolo[1,5-b]pyridazine and purine, and wherein said Het group may be substituted with one to three substituents selected from the group consisting of C₁-C₄ alkyl, phenyl, pyridyl, benzyl, C₁-C₄ alkoxy, methylthio, fluoro, chloro, nitro, cyano, hydroxy, oxo, amino, methylamino, dimethylamino, 2-dimethylaminoethyl, acetamido and acetyl; or

(d) 2,5-dioxo-l-imidazolidinyl or 2,4-dioxo-l-imidazolidinyl, which may be optionally substituted at the carbon atom by one or two methyl, linear or branched C₂-C₄ alkyl, phenyl, benzyl or hydroxymethyl groups, and at the nitrogen atom with C₁-C₄ linear or branched alkyl; and

n is 0 or 2,

said process comprising:

(A) hydrolysing said compound of formula 4 in which R is a residue of a carboxylic acid ester to give a compound of formula (I) in which X is HO-; or

(B) hydrolysing and oxidising, in either order, said compound of formula 4 in which n is 0 and R is the residue of a carboxylic acid ester, to give a compound of formula (I) in which X is HO-; or

(C) activating said compound of formula 4 wherein R is H and n is 2 to form an activated carboxy group, coupling the activated carboxy group with hydroxylamine or an O-

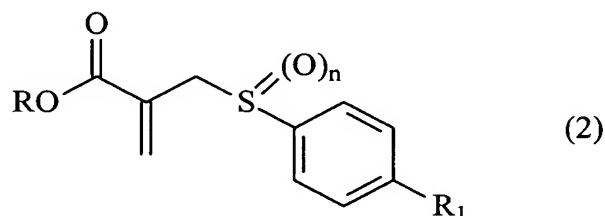
protected derivative thereof and, if necessary, deprotecting the hydroxamic group to give a compound of formula (I) wherein X is -NHOH; or

(D) submitting said compound of formula 4 wherein R is H and n is zero to a sequence of reactions comprising oxidation at the sulphur atom, activation of the carboxy group, condensation of the activated carboxy group with hydroxylamine or an O-protected derivative thereof and, if necessary, deprotection of the hydroxamic group to form a compound of formula (I) wherein X is -NHOH, the oxidation step being conducted either before the activation step or after the condensation step; and/or

(E) if desired, converting a resulting compound of formula (I) into another compound of formula (I); and/or converting a free compound into a pharmaceutically acceptable salt thereof; and/or converting a salt into a free compound.

A² 5. (Amended) The process according to claim 4 wherein the compound of formula 4 is obtained by

(A) subjecting a compound of formula 2:



wherein R is H or the residue of a carboxylic acid ester, R₁ is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, 4-cyanophenyl, benzamido and benzamido substituted on the terminal phenyl ring by C₁-C₄ alkyl, fluoro, chloro, cyano or C₁-C₄ alkoxy; and

n is 0 or 2

to conjugate addition by treatment with a compound of formula R_2H wherein R_2 is selected from:

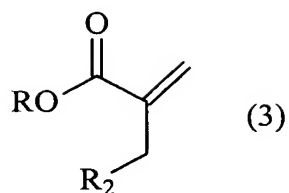
(a) $-S-Ar$ or $-S-CH_2-Ar$, wherein Ar is a monocarbocyclic or bicarbocyclic aromatic moiety which may be either unsubstituted or substituted with one or two substituents selected from the group consisting of C_1-C_4 alkyl, phenyl, benzyl, C_1-C_4 alkoxy, fluoro, chloro, bromo, nitro, cyano, hydroxy, amino, dimethylamino, acetamido, methylthio and acetyl;

(b) $-O-Ar$, wherein Ar is as defined above;

A² (c) $-S-Het$ or $-S-CH_2-Het$, wherein Het is a heterocyclic ring selected from the group consisting of pyridine, pyrimidine, pyridazine, pyrazine, 1,2,5-triazine, imidazole, thiophene, furan, pyrrole, pyrazole, 1,3-thiazole, 1,3-oxazole, 1,2,3-triazole, 1,2,4-triazole, 1,3,4-thiadiazole, 1,3,4-oxadiazole, 1,2,3,4-tetrazole, quinoline, isoquinoline, indole, 1,3-benzoxazole, 1,3-benzothiazole, benzimidazole, [1,3]oxazolo[4,5-b]pyridine, [1,3]thiazolo[4,5-b]pyridine, [1,2,3,4]tetrazolo[1,5-b]pyridazine and purine, and wherein said Het group may be substituted with one to three substituents selected from the group consisting of C_1-C_4 alkyl, phenyl, pyridyl, benzyl, C_1-C_4 alkoxy, methylthio, fluoro, chloro, nitro, cyano, hydroxy, oxo, amino, methylamino, dimethylamino, 2-dimethylaminoethyl, acetamido and acetyl; or

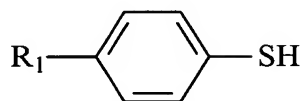
(d) 2,5-dioxo-1-imidazolidinyl or 2,4-dioxo-1-imidazolidinyl, which may be optionally substituted at the carbon atom by one or two methyl, linear or branched C_2-C_4 alkyl, phenyl, benzyl or hydroxymethyl groups, and at the nitrogen atom with C_1-C_4 linear or branched alkyl; or

(B) treating a compound of formula 3:



A² wherein R and R₂ are defined as above,

with a thiol of formula:



to obtain a compound of formula 4 in which n is zero.

6. (Amended) A pharmaceutical composition which comprises a pharmaceutically acceptable carrier or diluent and, as an active principle, the compound as defined in claim 1.

Please add the following new claims:

11. (New) A method of treating a mammal, including a human, comprising administering the compound claimed in claim 1, to said mammal, including a human, in need thereof.

A³ 12. (New) A method for treating a disease in a mammal, including a human, comprising administering an effective amount of the compound as claimed in claim 1, to said mammal, including a human, in need thereof, wherein said disease is a disease mediated by a matrix metalloproteinase.

13. (New) The method as claimed in claim 12, wherein the matrix metalloproteinase is selected from the group consisting of gelatinase (MMP-2), a membrane MMP involved in

gelatinase activation (MMP-14), a stromelysin (MMP-3 or MMP-10), collagenase (MMP-13) and neutrophyl collagenase (MMP-8).

14. (New) A method for the prevention of a disease in a mammal, including a human, comprising administering the compound claimed in claim 1, to said mammal, including a human, in need thereof, wherein said disease is a disease mediated by a matrix metalloproteinase.

15. (New) The method as claimed in claim 14, wherein the matrix metalloproteinase is selected from the group consisting of gelatinase (MMP-2), a membrane MMP involved in gelatinase activation (MMP-14), a stromelysin (MMP-3 or MMP-10), collagenase (MMP-13) and neutrophyl collagenase (MMP-8).

A3 16. (New) The method as claimed in claim 12, wherein the disease is selected from the group consisting of tumor growth, tumor metastasis, rheumatoid arthritis, osteoarthritis, ophthalmic disease, cardiovascular disease, periodontal disease, multiple sclerosis and Alzheimer's disease.

17. (New) The method as claimed in claim 14, wherein the disease is selected from the group consisting of tumor growth, tumor metastasis, rheumatoid arthritis, osteoarthritis, ophthalmic disease, cardiovascular disease, periodontal disease, multiple sclerosis and Alzheimer's disease.
